CLAIMS

What is claimed is:

1. The use of:

(a) 5,10 methylene tetrahydrofolate; and

(b) 5-fluorouracil or an analogue or prodrug thereof; and

(c) at least one additional chemotherapeutic agent,

in the manufacture of a pharmaceutical composition for the treatment of cancer, wherein the at least one additional chemotherapeutic agent is selected from the group consisting of:

an alkylating agent, an antimetabolite, a topoisomerase inhibitor, a microtubule disrupting drug, a nucleic acid synthesis inhibitor, a kinase inhibitor, a hormone blocking drug, a proteosome inhibitor, a vascularization inhibitor, an immune modulator, an anti-inflammatory, a cytokine, an inhibitor of a cytokine, a receptor-binding drug, and a 5-fluorouracil modulator.

2. The use of claim 1, wherein the cancer being treated is colorectal cancer, breast cancer, gastric cancer, non-small-cell lung cancer, cervical cancer, ovarian cancer, pancreatic cancer, esophageal cancer, or head-and-neck cancer.

3. The use of claim 1, wherein the at least one additional chemotherapeutic agent is a specific binding member, or a nucleic acid or a nucleic acid analogue molecule, or a small molecule.

4. The use of claim 3, wherein said specific binding member comprises an antibody that binds a growth factor.

5. The use of claim 4, wherein said antibody that binds a growth factor is at least one antibody that binds VEGF.

6. The use of claim 5, wherein the antibody the binds VEGF is bevacizumab.

7. The use of claim 3, wherein the specific binding member comprises an antibody that binds a growth factor receptor.

8. The use of claim 7, wherein the antibody that binds a growth factor is at least one antibody that binds EGFR.

9. The use of claim 8, wherein the antibody that binds EGFR is cetuximab.

10. The use of claim 1, wherein the at least one additional chemotherapeutic agent is selected from the group comprising: irinotecan (CPT-11]), difluorodeoxycytidine (gemcitabine), (E)-2'-deoxy-2'-(fluoromethylene) cytidine (tezacitabine), doxorubicin, epirubicin, mitomycin C, cyclophosphamide, cisplatin , oxaliplatin, paclitaxel, docetaxel, vincristine, vinblastine and vinorelbine.

11. The use of claim 1, wherein the pharmaceutical composition is formulated to be administered by injection or by intravenous feed.

12. The use of claim 1, wherein components (a), (b) and (c) of the pharmaceutical composition are formulated as a single formulation.

13. The use of claim 1, wherein components (a), (b) and (c) of the pharmaceutical composition are formulated separately.

14. A method of treating a patient with cancer, comprising administering 5-fluorouracil or an analogue or prodrug thereof; 5,10 methylene tetrahydrofolate; and at least one additional anticancer drug to a patient.

15. The method of claim 14, wherein 5-fluorouracil or an analogue or prodrug thereof is 5-fluorouracil.

16. The method of claim 15, wherein said 5-fluorouracil is administered by injection.

17. The method of claim 15, wherein the dosage of said 5-fluoruracil is from about 25 milligrams to about 5 grams per m^2.

18. The method of claim 17, wherein the dosage of said 5-fluoruracil is from about 50 milligrams to about 2.5 grams per m^2.

19. The method of claim 18, wherein the dosage of said 5-fluoruracil is from about 100 milligrams to about 1 gram per m^2.

20. The method of claim 14, wherein 5-fluorouracil or an analogue or prodrug thereof is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine).

21. The method of claim 20, wherein the daily dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 500 mg to about 7.5 grams per m^2.

22. The method of claim 21, wherein the dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 1000 mg to about 5 grams per m^2 .

23. The method of claim 22, wherein the dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 1500 mg to about 3000 mg per m^2.

24. The method of claim 14, wherein said 5,10 methylene tetrahydrofolate is administered by injection.

25. The method of claim 14, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 10 milligrams to 1 gram per m2.

26. The method of claim 25, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 20 milligrams to 500 milligrams per m2.

27. The method of claim 14, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 50 milligrams to 250 milligrams per m2.

28. The method of claim 14, wherein at least one of said at least one additional anticancer drug comprises at least one of: an alkylating agent, an antimetabolite, a topoisomerase inhibitor, a microtubule disrupting drug, a nucleic acid synthesis inhibitor, a kinase inhibitor, a hormone blocking drug, a proteosome inhibitor, a vascularization inhibitor, an immune modulator, an anti-inflammatory, a cytokine, an inhibitor of a cytokine, a receptor-binding drug, or a 5-fluorouracil modulator.

29. The method of claim 14, wherein at least one of said at least one additional anticancer drug comprises at least one of: a specific binding member, a nucleic acid or nucleic acid analogue molecule, or a small molecule.

30. The method of claim 1, wherein said cancer is colorectal cancer, breast cancer, gastric cancer, non-small-cell lung cancer, cervical cancer, ovarian cancer, pancreatic cancer, esophageal cancer, or head-and-neck cancer.

31. The method of claim 30, wherein said cancer is colorectal cancer.

32. The method of claim 30, wherein said cancer is breast cancer.

33. The method of claim 30, wherein said cancer is pancreatic cancer.

34. The method of claim 30, wherein said cancer is gastric cancer.

35. The method of claim 29, wherein at least one of said at least one additional anticancer drug comprises a specific binding member.

36. The method of claim 23, wherein said specific binding member comprises an antibody that binds binds VEGF.

37. The method of claim 36, wherein said antibody the binds VEGF is bevacizumab.

38. The method of claim 23, wherein said specific binding member comprises an antibody that binds EGFR.

39. The method of claim 38, wherein said antibody that binds EGFR is cetuximab.

40. The method of claim 28, wherein at least one of said at least one additional anticancer drug is a topoisomerase inhibitor.

41. The method of claim 40, wherein at least one of said at least one additional anticancer drug is irinotecan.

42. The method of claim 28, wherein at least one of said at least one additional anticancer drug is an antimetabolite.

43. The method of claim 42, wherein at least one of said at least one additional anticancer drug is difluorodeoxycytidine (gemcitabine), (E)-2'-deoxy-2'-(fluoromethylene) cytidine (tezacitabine), doxorubicin, or epirubicin.

44. The method of claim 38, wherein at least one of said at least one additional anticancer drug is an alkylating agent.

45. The method of claim 44, wherein at least one of said at least one additional anticancer drug is mitomycin C, cyclophosphamide, cisplatin or oxaliplatin.

46. The method of claim 45, wherein at least one of said at least one additional anticancer drug is oxaliplatin.

47. The method of claim 28, wherein at least one of said at least one additional anticancer drug is a kinase inhibitor.

48. The method of claim 47, said kinase inhibitor is a tyrosine kinase inhibitor.

49. The method of claim 48, wherein said tyrosine kinase inhibitor is an EGFR tyrosine kinase inhibitor or a VEGFR tyrosine kinase inhibitor.

50. The method of claim 28, wherein at least one of said at least one additional anticancer drug is a disruptor of microtubules.

51. The method of claim 50, wherein at least one of said at least one additional anticancer drug is paclitaxel, docetaxel, vincristine, vinblastine, or vinorelbine.

52. A method of reducing the toxicity of an anticancer drug regimen to be administered to a patient diagnosed with cancer, comprising:

obtaining an anticancer drug regimen that comprises:
5-fluorouracil or an analogue or prodrug thereof;
folinic acid; and
at least one additional anticancer drug; and

substituting 5,10 methylene tetrahydrofolate for folinic in the anticancer drug regime to be administered to the patient diagnosed with cancer

53. The method of claim 42, wherein said 5-fluorouracil or an analogue or prodrug thereof is 5-fluorouracil.

54. The method of claim 52, wherein said 5-fluorouracil or an analogue or prodrug thereof is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine).

55. The method of claim 52, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 10 milligrams to 1 gram per.

56. The method of claim 55, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 20 milligrams to 500 milligrams per m^2 .

57. The method of claim 56, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 30 milligrams to 250 milligrams per m^2 .

58. The method of claim 52, wherein at least one of said at least one additional anticancer drug comprises at least one of: an alkylating agent, an antimetabolite, a topoisomerase inhibitor, a microtubule disrupting drug, a nucleic acid synthesis inhibitor, a kinase inhibitor, a hormone blocking drug, a proteosome inhibitor, a vascularization inhibitor, an immune modulator, an anti-inflammatory, a cytokine, an inhibitor of a cytokine, a receptor-binding drug, or a 5-fluorouracil modulator.

59. The method of claim 52, wherein at least one of said at least one additional anticancer drug comprises at least one of: a specific binding member, a nucleic acid or nucleic acid analogue molecule, or a small molecule.

60. The method of claim 1, wherein said cancer is colorectal cancer, breast cancer, gastric cancer, Non-Small-Cell Lung Cancer, cervical cancer, ovarian cancer, pancreatic cancer, gastric cancer, or head-and-neck cancer.

61. The method of claim 60, wherein said cancer is colorectal cancer.

62. The method of claim 60, wherein said cancer is breast cancer.

63. The method of claim 60, wherein said cancer is pancreatic cancer.

64. The method of claim 60, wherein said cancer is gastric cancer.

65. The method of claim 49, wherein at least one of said at least one additional anticancer drug comprises a specific binding member.

66. The method of claim 65, wherein said specific binding member comprises an antibody that binds a growth factor.

67. The method of claim 66, wherein said antibody that binds a growth factor is at least one antibody that binds VEGF.

68. The method of claim 67, wherein said antibody that binds VEGF is bevacizumab.

69. The method of claim 65, wherein said antibody that binds a growth factor is at least one antibody that binds EGFR.

70. The method of claim 69, wherein said antibody that binds EGFR is certuximab.

71. The method of claim 58, wherein at least one of said at least one additional anticancer drug is a topoisomerase inhibitor.

72. The method of claim 71, wherein at least one of said at least one additional anticancer drug is irinotecan.

73. The method of claim 58, wherein at least one of said at least one additional anticancer drug is an antimetabolite.

74. The method of claim 73, wherein at least one of said at least one additional anticancer drug is difluorodeoxycytidine gemcitabine, (E)-2'-deoxy-2'-(fluoromethylene) cytidine (tezacitabine), doxorubicin or epirubicin.

75. The method of claim 58, wherein at least one of said at least one additional anticancer drug is an alkylating agent.

76. The method of claim 75, wherein at least one of said at least one additional anticancer drug is mitomycin C or cyclophosphamide.

77. The method of claim 75, wherein at least one of said at least one additional anticancer drug is cisplatin or oxaliplatin.

78. The method of claim 77, wherein at least one of said at least one additional anticancer drug is oxaliplatin.

79. The method of claim 58, wherein at least one of said at least one additional anticancer drug is a kinase inhibitor.

80. The method of claim 79, said kinase inhibitor is a tyrosine kinase inhibitor.

81. The method of claim 80, wherein said tyrosine kinase inhibitor is an EGFR tyrosine kinase inhibitor or a VEGFR tyrosine kinase inhibitor.

82. The method of claim 58, wherein at least one of said at least one additional anticancer drug is a disruptor of microtubules.

83. The method of claim 82, wherein at least one of said at least one additional anticancer drug is paclitaxel, docetaxel, vincristine, vinblastine, or vinorelbine.

84. A method of reducing the toxicity of an anticancer drug to be administered to a patient diagnosed with cancer; comprising:

obtaining an anticancer drug regimen that comprises:
5-fluorouracil or an analogue or prodrug thereof;
and at least one additional anticancer drug; and

adding 5,10 methylene tetrahydrofolate to the anticancer drug regime to be administered to the patient diagnosed with cancer.

85. The method of claim 84, wherein 5-fluorouracil or an analogue or prodrug thereof is 5-fluorouracil.

86. The method of claim 85, wherein said 5-fluorouracil is administered by injection.

87. The method of claim 85, wherein the dosage of said 5-fluoruracil is from about 25 milligrams to about 5 grams per m^2.

88. The method of claim 87, wherein the dosage of said 5-fluoruracil is from about 50 milligrams to about 2.5 grams per m^2.

89. The method of claim 88, wherein the dosage of said 5-fluoruracil is from about 100 milligrams to about 1 gram per m^2.

90. The method of claim 84, wherein 5-fluorouracil or an analogue or prodrug thereof is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine).

91. The method of claim 80, wherein the daily dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 500 mg to about 7.5 grams per m^2.

92. The method of claim 82, wherein the dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 1000 mg to about 5 grams per m^2.

93. The method of claim 83, wherein the dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 1500 mg to about 3000 mg per m^2.

94. The method of claim 84, wherein said 5,10 methylene tetrahydrofolate can be administered by injection.

95. The method of claim 84, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 10 milligrams to 1 gram per m^2.

96. The method of claim 95, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 20 milligrams to 500 milligrams per m^2.

97. The method of claim 96, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 30 milligrams to 250 milligrams per m^2.

98. The method of claim 84, wherein at least one of said at least one additional anticancer drug comprises at least one of: an alkylating agent, an antimetabolite, a topoisomerase inhibitor, a microtubule disrupting drug, a nucleic acid synthesis inhibitor, a kinase inhibitor, a hormone blocking drug, a proteosome inhibitor, a vascularization inhibitor, an immune modulator, an anti-inflammatory, a cytokine, an inhibitor of a cytokine, a receptor-binding drug, or a 5-fluorouracil modulator.

99. The method of claim 74, wherein at least one of said at least one additional anticancer drug comprises at least one of: a specific binding member, a nucleic acid or nucleic acid analogue molecule, or a small molecule.

100. The method of claim 84, wherein said cancer is colorectal cancer, breast cancer, gastric cancer, non-small-cell lung cancer, cervical cancer, ovarian cancer, pancreatic cancer, esophageal cancer, or head-and-neck cancer.

101. The method of claim 100, wherein said cancer is colorectal cancer.

102. The method of claim 100, wherein said cancer is breast cancer.

103. The method of claim 100, wherein said cancer is pancreatic cancer.

104. The method of claim 100, wherein said cancer is gastric cancer.

105. The method of claim 99, wherein at least one of said at least one additional anticancer drug comprises a specific binding member.

106. The method of claim 105, wherein said specific binding member comprises an antibody that binds a growth factor.

107. The method of claim 106, wherein said antibody that binds a growth factor is at least one antibody that binds VEGF.

108. The method of claim 107, wherein said antibody the binds VEGF is bevacizumab.

109. The method of claim 105, wherein said specific binding member comprises an antibody that binds a growth factor receptor.

110. The method of claim 109, wherein said antibody that binds a growth factor is at least one antibody that binds EGFR.

111. The method of claim 110, wherein said antibody that binds EGFR is cetuximab.

112. The method of claim 98, wherein at least one of said at least one additional anticancer drug is a topoisomerase inhibitor.

113. The method of claim 112, wherein at least one of said at least one additional anticancer drug is irinotecan.

114. The method of claim 98, wherein at least one of said at least one additional anticancer drug is an antimetabolite.

115. The method of claim 114, wherein at least one of said at least one additional anticancer drug is difluorodeoxycytidine (gemcitabine), (E)-2'-deoxy-2'-(fluoromethylene) cytidine (tezacitabine), doxorubicin, or epirubicin.

116. The method of claim 98, wherein at least one of said at least one additional anticancer drug is an alkylating agent.

117. The method of claim 116, wherein at least one of said at least one additional anticancer drug is mitomycin C, cyclophosphamide, cisplatin or oxaliplatin.

118. The method of claim 117, wherein at least one of said at least one additional anticancer drug is oxaliplatin.

119. The method of claim 98, wherein at least one of said at least one additional anticancer drug is a kinase inhibitor.

120. The method of claim 119, said kinase inhibitor is a tyrosine kinase inhibitor.

121. The method of claim 120, wherein said tyrosine kinase inhibitor is an EGFR tyrosine kinase inhibitor or a VEGFR tyrosine kinase inhibitor.

122. The method of claim 98, wherein at least one of said at least one additional anticancer drug is a disruptor of microtubules.

123. The method of claim 122, wherein at least one of said at least one additional anticancer drug is paclitaxel, docetaxel, vincristine, vinblastine, or vinorelbine.

124. A method of reducing the toxicity of an anticancer drug regimen administered to a patient with cancer; comprising:

obtaining an anticancer drug regimen that comprises:
an analogue or prodrug of 5-fluorouracil and folinic acid; and

substituting 5,10 methylene tetrahydrofolate for folinic acid in the anticancer drug regime to be administered to the patient diagnosed with cancer.

125. The method of claim 124, wherein said analogue or prodrug of 5-fluorouracil is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine).

126. The method of claim 125, wherein the daily dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 500 mg to about 7.5 grams per m^2.

127. The method of claim 126, wherein the dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 1000 mg to about 5 grams per m^2.

128. The method of claim 127, wherein the dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 200 mg to about 1500 mg per m^2 .

129 The method of claim 124, wherein said 5,10 methylene tetrahydrofolate can be administered by injection.

130. The method of claim 114, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 10 milligrams to 1 gram per m2.

131. The method of claim 121, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 20 milligrams to 500 milligrams per m2.

132. The method of claim 122, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 30 milligrams to 250 milligrams per m2.

133. A method of increasing the efficacy of an anticancer drug regimen to be administered to a patient diagnosed with cancer, comprising:

obtaining an anticancer drug regimen that comprises:
5-fluorouracil or an analogue or prodrug thereof;
folinic acid; and
at least one additional anticancer drug; and

substituting 5,10 methylene tetrahydrofolate for folinic in the anticancer drug regimen to be administered to the patient diagnosed with cancer.

134. The method of claim 133, wherein said 5-fluorouracil or an analogue or prodrug thereof is 5-fluorouracil.

135. The method of claim 134, wherein said 5-fluorouracil or an analogue or prodrug thereof is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine).

136. The method of claim 135, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 10 milligrams to 1 gram per m^2.

137. The method of claim 136, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 20 milligrams to 500 milligrams per m^2.

138. The method of claim 137, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 30 milligrams to 250 milligrams per m^2.

139. The method of claim 133, wherein at least one of said at least one additional anticancer drug comprises at least one of: an alkylating agent, an antimetabolite, a topoisomerase inhibitor, a microtubule disrupting drug, a nucleic acid synthesis inhibitor, a kinase inhibitor, a hormone blocking drug, a proteosome inhibitor, a vascularization inhibitor, an immune modulator, an anti-inflammatory, a cytokine, an inhibitor of a cytokine, a receptor-binding drug, or a 5-fluorouracil modulator.

140. The method of claim 133, wherein at least one of said at least one additional anticancer drug comprises at least one of: a specific binding member, a nucleic acid or nucleic acid analogue molecule, or a small molecule.

141. The method of claim 133, wherein said cancer is colorectal cancer, breast cancer, gastric cancer, Non-Small-Cell Lung Cancer, cervical cancer, ovarian cancer, pancreatic cancer, gastric cancer, or head-and-neck cancer.

142. The method of claim 133, wherein said cancer is colorectal cancer.

143. The method of claim 133, wherein said cancer is breast cancer.

144. The method of claim 133, wherein said cancer is pancreatic cancer.

145. The method of claim 133, wherein said cancer is gastric cancer.

146. The method of claim 140, wherein at least one of said at least one additional anticancer drug comprises a specific binding member.

147. The method of claim 146, wherein said specific binding member comprises an antibody that binds a growth factor.

148. The method of claim147, wherein said antibody that binds a growth factor is at least one antibody that binds VEGF.

149. The method of claim 148, wherein said antibody that binds VEGF is bevacizumab.

150. The method of claim 146, wherein said specific binding member is at least one antibody that binds EGFR.

151. The method of claim 141, wherein said antibody that binds EGFR is certuximab.

152. The method of claim 139, wherein at least one of said at least one additional anticancer drug is a topoisomerase inhibitor.

153. The method of claim 152, wherein at least one of said at least one additional anticancer drug is irinotecan.

154. The method of claim 139, wherein at least one of said at least one additional anticancer drug is an antimetabolite.

155. The method of claim 154, wherein at least one of said at least one additional anticancer drug is difluorodeoxycytidine (gemcitabine), (E)-2'-deoxy-2'-(fluoromethylene) cytidine (tezacitabine), doxorubicin or epirubicin.

156. The method of claim 139, wherein at least one of said at least one additional anticancer drug is an alkylating agent.

157. The method of claim 156, wherein at least one of said at least one additional anticancer drug is mitomycin C or cyclophosphamide.

158. The method of claim 156, wherein at least one of said at least one additional anticancer drug is cisplatin or oxaliplatin.

159. The method of claim 158, wherein at least one of said at least one additional anticancer drug is oxaliplatin.

160. The method of claim 139, wherein at least one of said at least one additional anticancer drug is a kinase inhibitor.

161. The method of claim 160, said kinase inhibitor is a tyrosine kinase inhibitor.

162. The method of claim 161, wherein said tyrosine kinase inhibitor is an EGFR tyrosine kinase inhibitor or a VEGFR tyrosine kinase inhibitor.

163. The method of claim 139, wherein at least one of said at least one additional anticancer drug is a disruptor of microtubules.

164. The method of claim 163, wherein at least one of said at least one additional anticancer drug is paclitaxel, docetaxel, vincristine, vinblastine, or vinorelbine.

165. A method of increasing the efficacy of an anticancer drug regimen to be administered to a patient diagnosed with cancer, comprising:

obtaining an anticancer drug regimen that comprises:

5-fluorouracil or an analogue or prodrug thereof

and

at least one additional anticancer drug; and

adding 5,10 methylene tetrahydrofolate to the anticancer drug regimen to be administered to the patient diagnosed with cancer.

166. The method of claim 165, wherein 5-fluorouracil or an analogue or prodrug thereof is 5-fluorouracil.

167. The method of claim 166, wherein said 5-fluorouracil can be administered by injection.

168. The method of claim 166, wherein the dosage of said 5-fluoruracil is from about 25 milligrams to about 5 grams per m^2.

169. The method of claim 168, wherein the dosage of said 5-fluoruracil is from about 50 milligrams to about 2.5 grams per m^2.

170. The method of claim 160, wherein the dosage of said 5-fluoruracil is from about 100 milligrams to about 1 gram per m^2.

171. The method of claim 165, wherein 5-fluorouracil or an analogue or prodrug thereof is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine).

173. The method of claim 171, wheren said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) can be administered in an oral formulation from one to six times daily.

174. The method of claim 163, wherein the daily dosage of said is N4-pentoxylcarbonyl -5'- deoxy-5-fluorocytidine (capecitabine) is from about 500 mg to about 7.5 grams per m^2.

175. The method of claim 174, wherein the daily dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 1000 mg to about 5 grams per m^2.

176. The method of claim 175, wherein the daily dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 1500 mg to about 3000 mg per m^2.

177. The method of claim 165, wherein said 5,10 methylene tetrahydrofolate can be administered by injection.

178. The method of claim 165, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 10 milligrams to 1 gram per m^2.

179. The method of claim 168, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 20 milligrams to 500 milligrams per m^2.

180. The method of claim 169, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 30 milligrams to 250 milligrams per m^2.

181. The method of claim 165, wherein at least one of said at least one additional anticancer drug comprises at least one of: an alkylating agent, an antimetabolite, a topoisomerase inhibitor, a microtubule disrupting drug, a nucleic acid synthesis

inhibitor, a kinase inhibitor, a hormone blocking drug, a proteosome inhibitor, a vascularization inhibitor, an immune modulator, an anti-inflammatory, a cytokine, an inhibitor of a cytokine, a receptor-binding drug, or a 5-fluorouracil modulator.

182. The method of claim 165, wherein at least one of said at least one additional anticancer drug comprises at least one of: a specific binding member, a nucleic acid or nucleic acid analogue molecule, or a small molecule.

183. The method of claim 165, wherein said cancer is colorectal cancer, breast cancer, gastric cancer, non-small-cell lung cancer, cervical cancer, ovarian cancer, pancreatic cancer, esophageal cancer, or head-and-neck cancer.

184. The method of claim 183, wherein said cancer is colorectal cancer.

185. The method of claim 183, wherein said cancer is breast cancer.

186. The method of claim 183, wherein said cancer is pancreatic cancer.

187. The method of claim 183, wherein said cancer is gastric cancer.

188. The method of claim 182, wherein at least one of said at least one additional anticancer drug comprises a specific binding member.

189. The method of claim 188, wherein said specific binding member comprises an antibody that binds a growth factor.

190. The method of claim 189, wherein said antibody that binds a growth factor is at least one antibody that binds VEGF.

191. The method of claim 190, wherein said antibody the binds VEGF is bevacizumab.

192. The method of claim 188, wherein said specific binding member comprises an antibody that binds a growth factor receptor.

193. The method of claim 192, wherein said antibody that binds a growth factor is at least one antibody that binds EGFR.

194. The method of claim 193, wherein said antibody that binds EGFR is cetuximab.

195. The method of claim 181, wherein at least one of said at least one additional anticancer drug is a topoisomerase inhibitor.

196. The method of claim 195, wherein at least one of said at least one additional anticancer drug is irinotecan.

197. The method of claim 181, wherein at least one of said at least one additional anticancer drug is an antimetabolite.

198. The method of claim 197, wherein at least one of said at least one additional anticancer drug is difluorodeoxycytidine (gemcitabine), (E)-2'-deoxy-2'-(fluoromethylene) cytidine (tezacitabine), doxorubicin, or epirubicin.

199. The method of claim 181, wherein at least one of said at least one additional anticancer drug is an alkylating agent.

200. The method of claim 199, wherein at least one of said at least one additional anticancer drug is mitomycin C, cyclophosphamide, cisplatin or oxaliplatin.

201. The method of claim 200, wherein at least one of said at least one additional anticancer drug is oxaliplatin.

202. The method of claim 181, wherein at least one of said at least one additional anticancer drug is a kinase inhibitor.

203. The method of claim 202, said kinase inhibitor is a tyrosine kinase inhibitor.

204. The method of claim 203, wherein said tyrosine kinase inhibitor is an EGFR tyrosine kinase inhibitor or a VEGFR tyrosine kinase inhibitor.

205. The method of claim 181, wherein at least one of said at least one additional anticancer drug is a disruptor of microtubules.

206. The method of claim 205, wherein at least one of said at least one additional anticancer drug is paclitaxel, docetaxel, vincristine, vinblastine, or vinorelbine.

207. A method of increasing the efficacy of an anticancer drug regimen administered to a patient with cancer; comprising:

obtaining an anticancer drug regimen that comprises:
an analogue or prodrug of 5-fluorouracil and folinic acid; and

substituting 5,10 methylene tetrahydrofolate for folinic acid in the anticancer drug regime to be administered to the patient diagnosed with cancer.

208. The method of claim 207, wherein said analogue or prodrug of 5-fluorouracil is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine).

209. The method of claim 208, wheren said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) can be administered in an oral formulation from one to six times daily.

210. The method of claim 208, wherein the dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 500 mg to about 7.5 grams per m^2.

211. The method of claim 200, wherein the dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 1000 mg to about 5 grams per m^2.

212. The method of claim 201, wherein the dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 1500 mg to about 3000 mg per m^2.

213. The method of claim 197, wherein said 5,10 methylene tetrahydrofolate can be administered by injection.

214. The method of claim 197, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 10 milligrams to 1 gram per m^2.

215. The method of claim 214, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 20 milligrams to 500 milligrams per m^2.

216. The method of claim 215, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 30 milligrams to 250 milligrams per m^2.

217. A method of increasing the efficacy of an anticancer drug regimen to be administered to a patient diagnosed with cancer, comprising:

obtaining an anticancer drug regimen that comprises:

5-fluorouracil or an analogue or prodrug thereof;

folinic acid; and

at least one additional anticancer drug;

substituting 5,10 methylene tetrahydrofolate for folinic acid in the anticancer drug regimen; and

increasing the dosage of the at least one additional anticancer drug in the anticancer drug regimen to obtain an anticancer drug regimen with increased efficacy.

218. The method of claim 217, wherein 5-fluorouracil or an analogue or prodrug thereof is 5-fluorouracil.

219. The method of claim 218, wherein said 5-fluorouracil is administered by injection.

220. The method of claim 208, wherein the dosage of said 5-fluoruracil is from about 25 milligrams to about 5 grams per m^2.

221. The method of claim 220, wherein the dosage of said 5-fluoruracil is from about 50 milligrams to about 2.5 grams per m^2.

222. The method of claim 221, wherein the dosage of said 5-fluoruracil is from about 100 milligrams to about 1 gram per m^2 .

223. The method of claim 217, wherein 5-fluorouracil or an analogue or prodrug thereof is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine).

224. The method of claim 223, wherein said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is administered in an oral formulation from one to six times daily.

225. The method of claim 223, wherein the daily dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 500 mg to about 7.5 grams per m^2.

226. The method of claim 225, wherein the dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 1000 mg to 5 grams per m^2 .

227. The method of claim 226, wherein the dosage of said is N4-pentoxylcarbonyl -5'-deoxy-5-fluorocytidine (capecitabine) is from about 1500 mg to about 3000 mg per m^2.

228. The method of claim 227, wherein said 5,10 methylene tetrahydrofolate is administered by injection.

229. The method of claim 217, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 10 milligrams to 1 gram per m^2 .

230. The method of claim 229, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 25 milligrams to 500 milligrams per m^2 .

231. The method of claim 220, wherein the dosage of said 5,10 methylene tetrahydrofolate is from about 50 milligrams to 250 milligrams per m^2 .

232. The method of claim 217, wherein at least one of said at least one additional anticancer drug comprises at least one of: an alkylating agent, an antimetabolite, a topoisomerase inhibitor, a microtubule disrupting drug, a nucleic acid synthesis inhibitor, a kinase inhibitor, a hormone blocking drug, a proteosome inhibitor, a vascularization inhibitor, an immune modulator, an anti-inflammatory, a cytokine, an inhibitor of a cytokine, a receptor-binding drug, or a 5-fluorouracil modulator.

233. The method of claim 217, wherein at least one of said at least one additional anticancer drug comprises at least one of: a specific binding member, a nucleic acid or nucleic acid analogue molecule, or a small molecule.

234. The method of claim 217, wherein said cancer is colorectal cancer, breast cancer, gastric cancer, non-small-cell lung cancer, cervical cancer, ovarian cancer, pancreatic cancer, esophageal cancer, or head-and-neck cancer.

235. The method of claim 234, wherein said cancer is colorectal cancer.

236. The method of claim 234, wherein said cancer is breast cancer.

237. The method of claim 234, wherein said cancer is pancreatic cancer.

238. The method of claim 234, wherein said cancer is gastric cancer.

239. The method of claim 233, wherein at least one of said at least one additional anticancer drug comprises a specific binding member.

240. The method of claim 239, wherein said specific binding member comprises an antibody that binds a growth factor.

241. The method of claim 240, wherein said antibody that binds a growth factor is at least one antibody that binds VEGF.

242. The method of claim 241, wherein said antibody the binds VEGF is bevacizumab.

243. The method of claim 239, wherein said specific binding member comprises an antibody that binds a growth factor receptor.

244. The method of claim 243, wherein said antibody that binds a growth factor is at least one antibody that binds EGFR.

245. The method of claim 234, wherein said antibody that binds EGFR is cetuximab.

246. The method of claim 232, wherein at least one of said at least one additional anticancer drug is a topoisomerase inhibitor.

247. The method of claim 246, wherein at least one of said at least one additional anticancer drug is irinotecan.

248. The method of claim 232, wherein at least one of said at least one additional anticancer drug is an antimetabolite.

249. The method of claim 248, wherein at least one of said at least one additional anticancer drug is difluorodeoxycytidine (gemcitabine), (E)-2'-deoxy-2'-(fluoromethylene) cytidine (tezacitabine), doxorubicin, or epirubicin.

250. The method of claim 232, wherein at least one of said at least one additional anticancer drug is an alkylating agent.

251. The method of claim 250, wherein at least one of said at least one additional anticancer drug is mitomycin C, cyclophosphamide, cisplatin or oxaliplatin.

252. The method of claim 241, wherein at least one of said at least one additional anticancer drug is oxaliplatin.

253. The method of claim 232, wherein at least one of said at least one additional anticancer drug is a kinase inhibitor.

254. The method of claim 253, said kinase inhibitor is a tyrosine kinase inhibitor.

255. The method of claim 254, wherein said tyrosine kinase inhibitor is an EGFR tyrosine kinase inhibitor or a VEGFR tyrosine kinase inhibitor.

256. The method of claim 232, wherein at least one of said at least one additional anticancer drug is a disruptor of microtubules.

257. The method of claim 256, wherein at least one of said at least one additional anticancer drug is paclitaxel, docetaxel, vincristine, vinblastine, or vinorelbine.